



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/473,551	12/28/1999	Jeffrey D. Milbrandt	6029-9879	1110

7590 02/22/2002
Elie H Gendloff
Howell & Haferkamp LC
7733 Forsyth Boulevard
Suite 1400
St. Louis, MO 63105

EXAMINER

CHERNYSHEV, OLGA N

ART UNIT

PAPER NUMBER 21

1646

DATE MAILED: 02/22/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/473,551

Applicant(s)

MILBRANDT ET AL.

Examiner

Olga N. Chernyshev

Art Unit

1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on _____.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 5-9 is/are pending in the application.
- 4a) Of the above claim(s) 5 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 and 6-9 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

Art Unit: 1646

DETAILED ACTION

1. Applicant's Petition from requirement for restriction under 37 C.F.R. 1.144 has been received. The petition will be forwarded for consideration.

Response to Amendment

2. Claims 1, 5-9 have been amended and claims 2-4 have been cancelled as requested in the amendment of Paper No.17, filed on December 17, 2001. Claims 1 and 5-9 are pending in the instant application.

Newly amended claim 5 is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: claim 5 is drawn to sequences not indicated as an elected invention by Applicant (see Paper No.11).

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 5 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 1 and 6-9 are examined in so far as they are drawn to the elected chimeric peptides of SEQ ID NO:23 and SEQ ID NO:26.

3. The Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action

Art Unit: 1646

4. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

5. Applicant's arguments filed on December 17, 2001 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Rejections - 35 USC § 112

6. Claims 1 and 6-9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention for the reasons explained in section 4 of Paper No.13.

Briefly, claims 1 and 6-9 are directed to a polypeptide which activates GFR α 1-RET but does not substantially activate GFR α 2-RET or GFR α 3-RET. Applicant has elected chimeric peptides of SEQ ID NO:23 and 26 as the polypeptides which activate GFR α 1-RET but which do not substantially activate GFR α 2-RET or GFR α 3-RET. However, the instant specification fails to provide any evidence or sound scientific reasoning that would support a conclusion that the claimed chimeric peptides of SEQ ID NO:23 and 26 possess such a function. The instant specification only teaches certain examples of such polypeptides, namely PGP-F2ac, PNP-F2ac and PAP-F2ac (see Examples of the instant specification and also Figure 6). Furthermore, on page 29 of the instant specification it is stated that "For this and other examples, the amino acid sequence of rat GDNF (SEQ ID NO:12) and mouse neurturin (SEQ ID NO:14) and persephin (SEQ ID NO:2), and human artemin (SEQ ID NO:15) were use for all constructs" (page 29, lines 16-18, emphasis added by the Examiner). Applicant's elected chimeric proteins are constructs of

Art Unit: 1646

SEQ ID NO:1 (human persephin) with the Fc and Fa regions comprising human GDNF F2c and F2a, respectively SEQ ID NO:20 and 17, such chimeric peptides thus comprising SEQ ID NO:23 and consisting of SEQ ID NO:26. Therefore, according to the instant specification the biological activity of the claimed peptides, such activity as to activate GFR α 1-RET but not to substantially activate GFR α 2-RET or GFR α 3-RET was never tested. Also, the instant specification has failed to point out those specific sequences that are responsible for differential activation ability of the claimed polypeptide, which would lead to an assumption that polypeptides of SEQ ID NO:23 or SEQ ID NO:26 might activate GFR α 1-RET but will not substantially activate GFR α 2-RET or GFR α 3-RET.

Applicant arguments regarding the ability of substituted human, mouse and rat persephin to operate as growth factors (page 4 of the Response) is misdirected in view, first, of the Applicant's elected invention of substituted human persephin, and, second, in view of the claims' amendment.

Applicant further argues that "structural similarity to a compound [...] [supports] an assertion of therapeutic utility for [another] compound" (page 4, third paragraph). The Examiner disagrees with this argument. It is well known in the art that changing even one amino acid in a protein sequence can lead to a new protein with new, sometimes significantly altered properties (Introduction to proteins and protein engineering. Robson, Garnier, 1986, p.41, second paragraph). It is also known and well described that amino acid structure cannot necessarily predict the function of the protein; see, for example, Skolnick et al.: "Knowing the protein structure by itself is insufficient to annotate a number of functional classes and is also insufficient for annotating the specific details of protein function" (Box 2 on page 36).

Applicant's reliance on *In re Brana*, 51 F.3d 1560,1566, 34 USPQ2d 1436 ,1441 (Fed. Cir. 1995) is misplaced. That court decision determined that a compound which belonged to a family of compounds known to have anti-tumor activity, which is a common and well established specific and substantial utility for that family of compounds, would be reasonably expected to have anti-tumor activity in light of positive *in vitro* data with respect to that particular compound since that data has proven to be an indicator of anti-cancer activity by other members of that family. The protein of the instant invention is a chimeric polypeptide with a particular claimed activity, but such activity cannot be simply extrapolated from the fact that a certain part of the claimed constructed polypeptide was derived from a protein having that activity when there is no evidence that constructed polypeptide is sufficient for that activity.

Conclusion

7. No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

Art Unit: 1646

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (703) 305-1003. The examiner can normally be reached on Monday to Friday 9 AM to 5 PM ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (703) 308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 782-9306 for regular communications and (703) 782-9307 for After Final communications.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 308-4556 or (703) 308-4242. If either of these numbers is out of service, please call the Group receptionist for an alternative number. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. Official papers should NOT be faxed to (703) 308-0294.

Art Unit: 1646

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Olga N. Chernyshev, Ph.D.
February 22, 2002

OC



JOHN ULM
PRIMARY EXAMINER
GROUP 1800